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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,829	03/29/2004	Alan D. King	04-100	9996

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EXAMINER	
FERNANDEZ, SUSAN EMILY	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/810,829	KING ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 25-50 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 25-50 is/are rejected.

7)☒ Claim(s) 32 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HL

DETAILED ACTION

The preliminary amendment filed March 29, 2004, has been received and entered.

Claims 25-50 are pending and are presented for examination.

Claim Objections

Claim 32 is objected to because it includes reference characters which are not enclosed within parentheses. Specifically, "42" is not enclosed within parentheses.

Reference characters corresponding to elements recited in the detailed description of the drawings and used in conjunction with the recitation of the same element or group of elements in the claims should be enclosed within parentheses so as to avoid confusion with other numbers or characters which may appear in the claims. See MPEP § 608.01(m).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-30, 32, 34, and 37-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29-30, 32, and 37-46 each recite "said static coating". There is no mention of "static coating" in the parent claim(s). Thus there is insufficient antecedent basis for this limitation in the claims. Therefore, claims 29-30, 32, and 37-47 are rejected under 35 U.S.C. 112, second paragraph.

Claims 38-46 each recite "said macromolecules". There is no mention of "macromolecules" in parent claim 25. Thus there is insufficient antecedent basis for this limitation in the claims. Therefore, claims 38-47 are rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25-27, 29-30, 37, 46-47, and 49-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Gross et al. (US Pat. 5,356,632).

Gross et al. discloses a transdermal drug delivery device comprising an anode electrode and a cathode electrode each coated with a gel containing a drug (column 3, lines 9-18). A gel is considered both a solid and a liquid (http://en.wikipedia.org/wiki/Gel). Different configurations of the drug delivery device are provided, including a configuration as shown in Figure 6. This configuration comprises multiple electrodes in parallel rows (column 4, line 58 through column 5, line 27). Furthermore, the drugs that may be delivered include beta-blockers and analgesics (column 3, lines 46-49).

Claims 49 and 50 are product-by-process claims. M.P.E.P. § 2113 reads, "Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps."

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)

The use of 35 U.S.C. §§ 102 and 103 rejections for product-by-process claims has been approved by the courts. "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable.

As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

A holding of anticipation is clearly required.

Claims 25, 29, 31-34, 37, 40-43, 46-47, and 49-50 are rejected under 35 U.S.C. 102(e) as being anticipated by Wang (US Pat. 6,514,762).

Wang discloses a device comprising two electrodes coated by nucleotides (column 2, lines 38-40) such as DNA and RNA (column 2, lines 65-67). The device allows for the delivery of nucleotides for "use in gene therapy for treatment or prevention of disease" (column 4, lines 16-19). Thus, Wang provides a method for DNA or RNA vaccine delivery, as a vaccine is used for disease prevention. In particular, the nucleotides may be used for treatment of cancer (column 8, lines 5-7).

Furthermore, the electrodes disclosed include metallic electrodes and metal-coated crystal wafer electrodes (column 5, lines 63-67). Thus, the electrode may have a fixed electrode surface that includes solid metal particles. In order to prepare the drug delivery device, the electrodes are immersed in solution containing the nucleotides, the electrodes are removed from the solution, and then allowed to dry (column 6, lines 41-60). Therefore, a solid coating of nucleotide is disposed on the electrodes (column 6, lines 60-61). The coating is also considered a liquid that had been fixed onto the electrode. Additionally, a positive charge or potential can be applied to the electrodes while the electrodes are in the nucleotide-containing solution (column 7, lines 32-41).

While Wang teaches claims 49 and 50, they are considered product-by-process claims. See discussion above.

A holding of anticipation is clearly required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 25-30, 37, and 46-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Hofmann (US Pat. 6,009,347).

Gross et al. discloses a transdermal drug delivery device comprising an anode electrode and a cathode electrode each coated with a gel containing a drug (column 3, lines 9-18). A gel is considered both a solid and a liquid (http://en.wikipedia.org/wiki/Gel). Different

configurations of the drug delivery device are provided, including a configuration as shown in Figure 6. This configuration comprises multiple electrodes in parallel rows (column 4, line 58 through column 5, line 27). Furthermore, the drugs that may be delivered include beta-blockers and analgesics (column 3, lines 46-49).

Claims 49 and 50 are product-by-process claims. M.P.E.P. § 2113 reads, "Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps."

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)

The use of 35 U.S.C. §§ 102 and 103 rejections for product-by-process claims has been approved by the courts. "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of

the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Gross et al. does not expressly disclose needle electrodes for drug delivery.

Hofmann discusses electroporation for use in introducing foreign material into living cells (column 1, lines 9-14 and lines 34-40). Specifically, Hofmann discloses using needle electrodes (column 4, lines 33-35) and notes that "the applicant has found through experimentation that pulsing between multiple pairs of electrodes in a multiple electrode array, preferably set up in rectangular or square patterns, provides improved results over that of pulsing between a pair of electrodes" (column 4, lines 49-53). The electroporation device may comprise of an array of needles as electrodes (column 4, lines 53-61).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use needle electrodes in the Gross drug delivery device.

One of ordinary skill in the art would have been motivated to do this because Hofmann indicates that needle-shaped electrodes allow for access to more deeply located cells (column 1, lines 44-45). A holding of obviousness is clearly required.

Claims 25-27, 29-34, 37, 46-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Meserol (US Pat. 6,090,617).

Gross et al. discloses a transdermal drug delivery device comprising an anode electrode and a cathode electrode each coated with a gel containing a drug. A gel is considered both a solid and a liquid. Different configurations of the drug delivery device are provided, including a configuration as shown in Figure 6. This configuration comprises electrodes in multiple electrodes in parallel rows. Furthermore, the drugs that may be delivered include beta-blockers and analgesics.

Claims 49 and 50 are product-by-process claims. See discussion above.

Gross et al. does not expressly disclose an electrode comprising a fixed electrode surface which is coated with a static layer of electrode releasable molecules.

Meserol discloses electrodes coated with a metal nitride coating for use in a saline solution. See abstract.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use the metal nitride coated electrodes disclosed in Meserol for use in the Gross drug delivery device.

One of ordinary skill in the art would have been motivated to do this because Meserol points out that metal nitride coatings "protect surgical implants or instruments used in a biological system from corrosion and wearing due to externally generated forces, such as salts or friction" (column 1, lines 46-49). Meserol provides an improved metal nitride coated electrode which addresses problems concerning electric signal generation or stimulation in biological systems as described in column 1, lines 54-59. Moreover, the electrodes disclosed in Meserol

"have substantially longer useful lives than conventional electrodes, due to their increased resistance to erosion and pitting normally caused by electrical signals emanating therefrom" (column 8, lines 54-57). Thus these coated electrodes would be desirable for use in practicing the Gross invention, where the electrodes are used for drug delivery in biological solutions or tissues. A holding of obviousness is clearly required.

Claims 25-27, 29-30, 35, 37, 46-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Vadgama et al. (WO 92/05434).

Gross et al. discloses a transdermal drug delivery device comprising an anode electrode and a cathode electrode each coated with a gel containing a drug. A gel is considered both a solid and a liquid. Different configurations of the drug delivery device are provided, including a configuration as shown in Figure 6. This configuration comprises multiple electrodes in parallel rows. Furthermore, the drugs that may be delivered include beta-blockers and analgesics.

Claims 49 and 50 are product-by-process claims. See discussion above.

Gross et al. does not expressly disclose an electrode comprising a fixed electrode surface which includes a liposome matrix.

Vadgama et al. discloses an electrode enclosed within liposomes (claim 1).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use the Vadgama electrodes in practicing the Gross invention, where electrodes enclosed within liposomes are coated with a static layer of electrode releasable molecules.

One of ordinary skill in the art would have been motivated to do this because it would have minimized corrosion of the electrode in biological solutions. A holding of obviousness is clearly required.

Claims 25-27, 29-30, 36-37, 46-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Hoffmann et al. (US Pat. 5,902,329).

Gross et al. discloses a transdermal drug delivery device comprising an anode electrode and a cathode electrode each coated with a gel containing a drug. A gel is considered both a solid and a liquid. Different configurations of the drug delivery device are provided, including a configuration as shown in Figure 6. This configuration comprises multiple electrodes in parallel rows. Furthermore, the drugs that may be delivered include beta-blockers and analgesics.

Claims 49 and 50 are product-by-process claims. See discussion above.

Gross et al. does not expressly disclose an electrode comprising a fixed electrode surface which includes a solid polymer matrix.

Hoffmann et al. discloses a device comprising electrodes coated with a hydrogel (see Figures 5 and 6 and column 8, lines 6-24). The hydrogel is defined as a polymer (column 6, lines 63-64), and may be used in drug delivery. Moreover, use of the hydrogel for drug delivery can be accomplished by "chemical binding a drug such as antibiotic, antiseptic, antiarrhythmic, anti-inflammatory steroid or other agents, to the polymer network" (column 7, lines 8-13). Thus the electrodes are coated with a polymer which can be coated with drugs.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to include in the Gross invention a solid polymer matrix as a fixed surface on the electrodes.

One of ordinary skill in the art would have been motivated to do this because Hoffmann et al. notes that "polymer hydrogels and other coatings have also been recommended for use on implantable devices to stimulate the attachment of endothelial cells for improving thromboresistance" (column 3, line 66 through column 4, line 2). Additionally, a polymer coating would prevent tissue ingrowth and minimize corrosion of electrodes in biological solutions and tissues. A holding of obviousness is clearly required.

Claims 25-27, 29-30, 37-43, 46-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Zewert et al. (US Pat. 5,749,847) and/or Widera et al. (Journal of Immunology, 2000, 164: 4635-4640).

Gross et al. discloses a transdermal drug delivery device comprising an anode electrode and a cathode electrode each coated with a gel containing a drug. A gel is considered both a solid and a liquid. Different configurations of the drug delivery device are provided, including a configuration as shown in Figure 6. This configuration comprises electrodes in multiple electrodes in parallel rows. Furthermore, the drugs that may be delivered include beta-blockers and analgesics.

Claims 49 and 50 are product-by-process claims. See discussion above.

Gross et al. does not expressly disclose the delivery of vaccines, including polynucleotide, DNA, and RNA vaccines.

Zewert et al. teaches the use of electroporation for the delivery of nucleotides into an organism (column 2, lines10-14). More specifically, a composition comprising the nucleotide(s) is applied to the skin, and the skin is subsequently electroporated. The composition applied to the epidermis for drug delivery may include a vaccine (column 4, lines 32-34), and appropriate nucleotides for delivery include polynucleotides, deoxyribonucleotides (column 3, lines 44-46), and ribonucleic acid (column 4, lines 44-46).

Widera et al. discloses DNA vaccine delivery facilitated by electroporation (abstract). Needle array electrodes were used for electroporation following the injection of DNA or a DNA vaccine (page 4636, first column, "DNA immunization and in vivo electroporation").

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use polynucleotide, DNA, and RNA vaccines as drugs to be delivered when practicing the Gross invention.

One of ordinary skill in the art would have been motivated to do this because the Gross invention involves electroporation for drug delivery, offering a device which accomplishes in a single step the methods of Zewert et al. and procedures performed in Widera et al. Moreover, Widera et al. concludes that "in vivo electroporation substantially increases DNA delivery and DNA vaccine potency, appears to be well tolerated by the animals, and is a simple technique that takes only a few seconds after inoculation" (page 4640, second paragraph). A holding of obviousness is clearly required.

Claims 25-27, 29-30, 37, 44-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Lerner (WO 97/18855).

Gross et al. discloses a transdermal drug delivery device comprising an anode electrode and a cathode electrode each coated with a gel containing a drug. A gel is considered both a solid and a liquid. Different configurations of the drug delivery device are provided, including a configuration as shown in Figure 6. This configuration comprises multiple electrodes in parallel rows. Furthermore, the drugs that may be delivered include beta-blockers and analgesics.

Claims 49 and 50 are product-by-process claims. See discussion above.

Gross et al. does not expressly disclose the delivery of protein-based vaccines.

Lerner discloses a drug delivery device comprising electrodes supporting a "drug or other biologically active substance or compound" (claim 9). Furthermore, drugs or other biologically active substances for delivery include bacterial vaccines (page 28, line 7), proteins (page 28, line 19), and viral vaccines (page 28, line 22).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to deliver protein-based vaccines when practicing the Gross invention.

One of ordinary skill in the art would have been motivated to do this because Lerner teaches that a variety of drugs can be delivered when using electrodes. It would have been desirable to deliver protein-based drugs for vaccination of bacterial and viral diseases. A holding of obviousness is clearly required.

Claims 25-27, 29-34, 37, 40-43, 46-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang in view of Gross et al.

Wang discloses a device comprising two electrodes coated by nucleotides (column 2, lines 38-40) such as DNA and RNA (column 2, lines 65-67). The device allows for the delivery of nucleotides for "use in gene therapy for treatment or prevention of disease" (column 4, lines 16-19). Thus, Wang provides a method for DNA or RNA vaccine delivery, as a vaccine is used for disease prevention. In addition, the nucleotides may be used for treatment of cancer (column 8, lines 5-7).

The electrodes used include metallic electrodes and metal-coated crystal wafer electrodes (column 5, lines 63-67). Thus, the electrode may have a fixed electrode surface that includes solid metal particles. In order to prepare the drug delivery device, the electrodes are immersed in solution containing the nucleotides, the electrodes are removed from the solution, and then allowed to dry (column 6, lines 41-60). Therefore, a solid coating of nucleotide is disposed on the electrodes (column 6, lines 60-61). The coating is also considered a liquid that had been fixed onto the electrode. Additionally, a positive charge or potential can be applied to the electrodes while the electrodes are in the nucleotide-containing solution (column 7, lines 32-41).

While Wang teaches claims 49 and 50, they are considered product-by-process claims. See discussion above.

Wang does not expressly disclose an electrode assembly or the presence of the nucleotides on the electrodes in a gel layer.

Gross et al. teaches a drug delivery device wherein a possible configuration comprises multiple electrodes in parallel rows (Figure 6 and column 4, line 58 through column 5, line 27). Furthermore, the drug to be delivered is in a gel.

At the time to the invention was made, it would have been obvious to a person of ordinary skill in the art to include more than two electrodes in the Wang invention in order to form an electrode assembly where there are parallel rows of electrodes, as was done in the Gross invention. Furthermore, it would have been obvious to use a gel as the nucleotide-containing layer on the electrodes.

One of ordinary skill in the art would have been motivated to do this because Gross et al. notes that the electrode assembly configuration comprising groups of electrodes shown in Figure 6 "enables the electrodes of each group to be selectively energized at different times (and also with different current magnitudes) for purposes of dispensing the drug of the gel layer...in the respective area at different times (and at different rates, if desired)" (column 4, line 65 through column 5, line 2). This would have been desirable because the initiation time and rate of drug delivery is critical in treatment of diseases/infections. Additionally, one would have been motivated to have used a gel layer as the nucleotide-containing layer on the electrodes since it would have altered the rate of release of the nucleotide to a more desirable rate. A holding of obviousness is clearly required.

Claims 25-34, 37, 40-43, and 46-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang and Gross et al. as applied to claims 25-27, 29-34, 37, 40-43, 46-47, and 49-50 above, and further in view of Hofmann (US Pat. 6,009,347).

As discussed above, Wang and Gross et al. render claims 25-27, 29-34, 37, 40-43, 46-47, and 49-50 obvious.

These references do not disclose needle electrodes for drug delivery.

Hofmann discusses electroporation for use in introducing foreign material into living cells (column 1, lines 9-14 and lines 34-40). Specifically, Hofmann discloses needle electrodes for use in electroporation (column 4, lines 33-35) and notes that "the applicant has found through experimentation that pulsing between multiple pairs of electrodes in a multiple electrode array, preferably set up in rectangular or square patterns, provides improved results over that of pulsing between a pair of electrodes" (column 4, lines 49-53). The electroporation device may comprise of an array of needles as electrodes (column 4, lines 53-61).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use needle electrodes in the Wang nucleotide delivery device.

One of ordinary skill in the art would have been motivated to do this because Hofmann indicates that needle-shaped electrodes allow for access to more deeply located cells (column 1, lines 44-45). This would have made the Wang device more suitable in delivering nucleotides to deep tissues. A holding of obviousness is clearly required.

Claims 25, 29, 31-35, 37, 40-43, 46-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang in view of Vadgama et al.

Wang discloses a device comprising two electrodes coated by nucleotides (column 2, lines 38-40) such as DNA and RNA (column 2, lines 65-67). The device allows for the delivery of nucleotides for "use in gene therapy for treatment or prevention of disease" (column 4, lines 16-19). Thus, Wang provides a method for DNA or RNA vaccine delivery, as a vaccine is used for disease prevention. In addition, the nucleotides may be used for treatment of cancer (column 8, lines 5-7).

The electrodes used include metallic electrodes and metal-coated crystal wafer electrodes (column 5, lines 63-67). Thus, the electrode may have a fixed electrode surface that includes solid metal particles. In order to prepare the drug delivery device, the electrodes are immersed in solution containing the nucleotides, the electrodes are removed from the solution, and then allowed to dry (column 6, lines 41-60). Therefore, a solid coating of nucleotide is disposed on the electrodes (column 6, lines 60-61). The coating is liquid that had been fixed onto the electrode. Additionally, a positive charge or potential can be applied to the electrodes while the electrodes are in the nucleotide-containing solution (column 7, lines 32-41).

While Wang teaches claims 49 and 50, they are considered product-by-process claims. See discussion above.

Wang does not expressly disclose an electrode comprising a fixed electrode surface which includes a liposome matrix.

Vadgama et al. discloses an electrode enclosed within liposomes (claim 1).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use the Vadgama electrodes in practicing the Gross invention, where electrodes enclosed within liposomes are coated with a static layer of electrode releasable molecules.

One of ordinary skill in the art would have been motivated to do this because it would have minimized corrosion of the electrode in biological solutions. A holding of obviousness is clearly required.

Claims 25, 29, 31-35, 37, 40-43, 46-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang in view of Hoffmann et al. (US Pat. 5,902,329).

Wang discloses a device comprising two electrodes coated by nucleotides (column 2, lines 38-40) such as DNA and RNA (column 2, lines 65-67). The device allows for the delivery of nucleotides for "use in gene therapy for treatment or prevention of disease" (column 4, lines 16-19). Thus, Wang provides a method for DNA or RNA vaccine delivery, as a vaccine is used for disease prevention. In addition, the nucleotides may be used for treatment of cancer (column 8, lines 5-7).

The electrodes used include metallic electrodes and metal-coated crystal wafer electrodes (column 5, lines 63-67). Thus, the electrode may have a fixed electrode surface that includes solid metal particles. In order to prepare the drug delivery device, the electrodes are immersed in solution containing the nucleotides, the electrodes are removed from the solution, and then allowed to dry (column 6, lines 41-60). Therefore, a solid coating of nucleotide is disposed on the electrodes (column 6, lines 60-61). The coating is also considered a liquid that had been fixed onto the electrode. Additionally, a positive charge or potential can be applied to the electrodes while the electrodes are in the nucleotide-containing solution (column 7, lines 32-41).

While Wang teaches claims 49 and 50, they are considered product-by-process claims. See discussion above.

Wang does not expressly disclose an electrode comprising a fixed electrode surface which includes a solid polymer matrix.

Hoffmann et al. discloses a device comprising electrodes coated which a hydrogel (see Figures 5 and 6 and column 8, lines 6-24). The hydrogel is defined as a polymer (column 6, lines 63-64), and may be used in drug delivery. Moreover, use of the hydrogel for drug delivery can be accomplished by "chemical binding a drug such as antibiotic, antiseptic, antiarrhythmic,

anti-inflammatory steroid or other agents, to the polymer network" (column 7, lines 8-13). Thus the electrodes are coated with a polymer which can be coated with drugs.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to include in the Wang invention a solid polymer matrix as a fixed surface on the electrodes.

One of ordinary skill in the art would have been motivated to do this because Hoffmann et al. notes that "polymer hydrogels and other coatings have also been recommended for use on implantable devices to stimulate the attachment of endothelial cells for improving thromboresistance" (column 3, line 66 through column 4, line 2). Additionally, a polymer coating would have prevented tissue ingrowth and would have minimized corrosion of electrodes in biological solutions and tissues. A holding of obviousness is clearly required.

Claims 25, 29, 31-34, 37-43, 46-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang in view of Zewert et al. and/or Widera et al.

Wang discloses a device comprising two electrodes coated by nucleotides (column 2, lines 38-40) such as DNA and RNA (column 2, lines 65-67). The device allows for the delivery of nucleotides for "use in gene therapy for treatment or prevention of disease" (column 4, lines 16-19). Thus, Wang provides a method for DNA or RNA vaccine delivery, as a vaccine is used for disease prevention. In addition, the nucleotides may be used for treatment of cancer (column 8, lines 5-7).

The electrodes used include metallic electrodes and metal-coated crystal wafer electrodes (column 5, lines 63-67). Thus, the electrode may have a fixed electrode surface that includes

solid metal particles. In order to prepare the drug delivery device, the electrodes are immersed in solution containing the nucleotides, the electrodes are removed from the solution, and then allowed to dry (column 6, lines 41-60). Therefore, a solid coating of nucleotide is disposed on the electrodes (column 6, lines 60-61). The coating is also considered a liquid that had been fixed onto the electrode. Additionally, a positive charge or potential can be applied to the electrodes while the electrodes are in the nucleotide-containing solution (column 7, lines 32-41).

While Wang teaches claims 49 and 50, they are considered product-by-process claims. See discussion above.

Wang does not expressly disclose the delivery of vaccines, including polynucleotide, DNA, and RNA vaccines.

Zewert et al. teaches the use of electroporation for the delivery of nucleotides into an organism (column 2, lines10-14). More specifically, a composition comprising the nucleotide(s) is applied to the skin, and the skin is subsequently electroporated. The composition applied to the epidermis for drug delivery may include a vaccine (column 4, lines 32-34), and appropriate nucleotides for delivery include polynucleotides, deoxyribonucleotides (column 3, lines 44-46), and ribonucleic acid (column 4, lines 44-46).

Widera et al. discloses DNA vaccine delivery facilitated by electroporation (abstract). Needle array electrodes were used for electroporation following the injection of DNA or a DNA vaccine (page 4636, first column, "DNA immunization and in vivo electroporation").

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use polynucleotide, DNA, and RNA vaccines as nucleotide compositions to be delivered when practicing the Wang invention.

One of ordinary skill in the art would have been motivated to do this because the Wang invention involves electroporation for nucleotide delivery, offering a device which accomplishes in a single step the methods of Zewert et al. and procedures performed in Widera et al. Moreover, Widera et al. concludes that "in vivo electroporation substantially increases DNA delivery and DNA vaccine potency, appears to be well tolerated by the animals, and is a simple technique that takes only a few seconds after inoculation" (page 4640, second paragraph). A holding of obviousness is clearly required.

Claims 25, 29, 31-34, 37, 40-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang in view of Lerner.

Wang discloses a device comprising two electrodes coated by nucleotides (column 2, lines 38-40) such as DNA and RNA (column 2, lines 65-67). The device allows for the delivery of nucleotides for "use in gene therapy for treatment or prevention of disease" (column 4, lines 16-19). Thus, Wang provides a method for DNA or RNA vaccine delivery, as a vaccine is used for disease prevention. In addition, the nucleotides may be used for treatment of cancer (column 8, lines 5-7).

The electrodes used include metallic electrodes and metal-coated crystal wafer electrodes (column 5, lines 63-67). Thus, the electrode may have a fixed electrode surface that includes solid metal particles. In order to prepare the drug delivery device, the electrodes are immersed in solution containing the nucleotides, the electrodes are removed from the solution, and then allowed to dry (column 6, lines 41-60). Therefore, a solid coating of nucleotide is disposed on the electrodes (column 6, lines 60-61). The coating is also considered a liquid that had been

fixed onto the electrode. Additionally, a positive charge or potential can be applied to the electrodes while the electrodes are in the nucleotide-containing solution (column 7, lines 32-41).

While Wang teaches claims 49 and 50, they are considered product-by-process claims. See discussion above.

Wang does not expressly disclose the delivery of protein-based vaccines.

Lerner discloses a drug delivery device comprising electrodes supporting a "drug or other biologically active substance or compound" (claim 9). Furthermore, drugs or other biologically active substances for delivery include bacterial vaccines (page 28, line 7), proteins (page 28, line 19), and viral vaccines (page 28, line 22).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to deliver protein-based vaccines when practicing the Wang invention.

One of ordinary skill in the art would have been motivated to do this because Lerner teaches that a variety of drugs can be delivered when using electrodes. It would have been desirable to deliver protein-based drugs for vaccination of bacterial and viral diseases. There would have been a reasonable expectation of success in the substitution of protein-based vaccine as the drug to be delivered in practicing the Wang invention. A holding of obviousness is clearly required.

No claim are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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